Intro to Autonomics

Introduction

The **autonomic nervous system** (ANS) comprises two physiologically competing systems. The **sympathetic nervous system** (SNS) is the activating, **fight-or-flight**, high-anxiety, stressed system that heightens awareness, increases heart rate, increases blood pressure, and prepares for danger. The **parasympathetic nervous system** (PNS) is the **rest-and-digest** system, low-anxiety, low-sphincter-tone, relaxed mode. These two together are called **autonomic** because it's **self-governing and self-acting**—we have no conscious control over it. Although there are **additional somatic** controls over some of these systems (you can "hold in" your urine or stool), the autonomic system operates automatically, without our control or say-so.

This system is also ripe for the exam because there are two opposing physiologic systems that capitalize on several different receptor types. Because it's so well studied, we have drugs that activate or inactivate each of these receptors. That means the test can assess your knowledge of normal functioning, abnormal functioning, what happens when there are lesions to the system, and what happens when a drug is added to the system. There are so many permutations, it becomes **incredibly difficult to memorize**. However, if you learn the function of the system, the answer to scenarios is **likewise incredibly easy to deduce.** Although we talk here about the anatomy and physiology of the system as a whole, many of the test questions come from what happens to the **cardiovascular system** and what happens to the **eye.** Let's start with the system as a whole, then get into the details.

Similarities of SNS and PNS: Preganglionic Synapses

The entirety of the ANS is built on a first-order neuron coming from the central nervous system, synapsing onto a second-order neuron in the periphery, which then finally synapses on its target, the effector organ.

The first-order neurons (coming from the central nervous system) are called **preganglionic neurons**. Where preganglionic neurons synapse with second-order neurons is called a **ganglion.** The ganglia are outside the central nervous system, in the periphery. This synapse is called the **preganglionic synapse.** A ganglion is a collection of neurons; a sort of meeting-up point. Multiple first-order neurons enter a ganglion from the central nervous system and multiple second-order neurons leave it for the target organ. From the ganglion, those second-order neurons, called **postganglionic neurons**, travel through tissue to their target organ, the **effector organ**. The synapse on the effector organ is called the **postganglionic synapse** or the **effector synapse**.

All **preganglionic neurons** release acetylcholine (**ACh**), and all **postganglionic neurons** have **nicotinic** acetylcholine receptors. Regardless of SNS or PNS, whether the SNS is innervating a ganglion or the medulla, no matter where we are in the body, everywhere and always within the autonomic nervous system, the first synapse from preganglionic to postganglionic tissue uses the neurotransmitter **acetylcholine and it goes to a nicotinic acetylcholine receptor**.

All SNS preganglionic neurons release ACh, whether they release onto the adrenal medulla or to a second-order neuron. All SNS cells that receive an ACh-based signal from a preganglionic neuron have nicotinic ACh receptors. This setup is identical to the PNS.

The similarities end there. The SNS and PNS don't like each other. There are **SNS ganglia** and there are **PNS ganglia**—they never hang out together. In fact, the SNS and PNS are directly at war with each other. They originate at different places in the central nervous system (CNS), they synapse at different ganglia than one another, and they have opposing physiologic effects. The postganglionic neurotransmitter to the effector organ is different, and the impact on effector organs is different.

Autonomics as a Whole: Physiologic Balance

Balance between the SNS and PNS is maintained by **tone**. Tone means how activated a system is. That is to say, the systems are **not ON/OFF** but operate on a **sliding scale**—both are always on. If a given system were already in balance, one could tip the system in favor of the SNS **either by ramping up the SNS** or by **slowing down the PNS**. The body shifts emphasis to either the SNS or PNS by **increasing or decreasing tone** on a given system. More stimulation, more ganglionic synapses (more tone) on the SNS than on the PNS lets the SNS win; less firing, fewer ganglionic synapses firing (less tone) on the PNS than on the SNS will also let the SNS win. The same is true in reverse—more PNS or less SNS lets the PNS win.

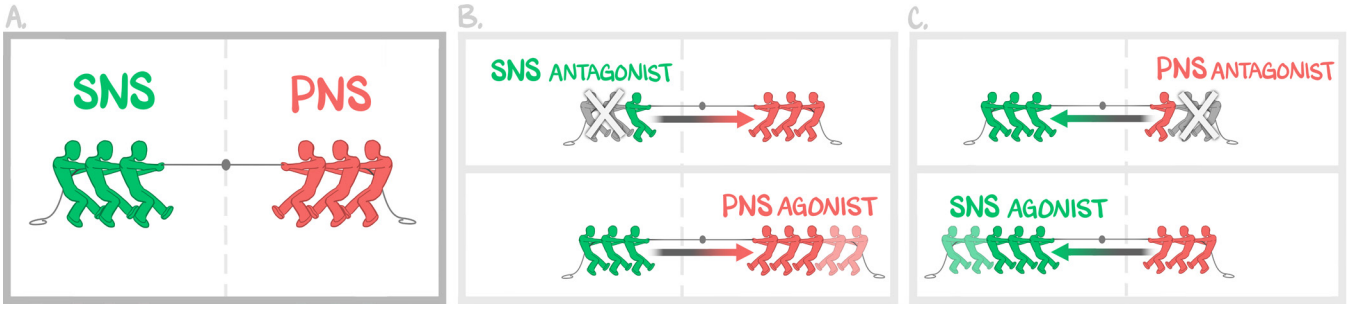

Figure 8.1: Balance and Tone
With a system in balance—equal tone for SNS and PNS—the balance can be shifted towards one or the other by two complementary methods: adding tone to the one or removing it from the other. This means that because there is constant tone, agonist drugs and antagonist drugs both work, so that antagonizing the PNS or agonizing the SNS shifts the system towards the SNS, whereas antagonizing the SNS or agonizing the PNS shifts the system towards the PNS.

The Difference between SNS and PNS: Anatomy

The **PNS** arises from the brain stem and the caudal end of the spinal cord. The brain stem parasympathetics originate from the brain stem and so originate rostral then **stay rostral**, synapsing on rostral ganglia. The fibers are individual, **do not form a trunk**, and so stay separate from the rostral PNS. The **caudal PNS originates** from **S1 to S4** and remains rostral, synapsing on rostral ganglia. The fibers are individual, **do not form a trunk**, and so stay separate from the caudal PNS. They're the same system, they're controlled by the same reflexes, but consider them as two distinct anatomic locations. This is especially relevant when there's an injury to the spinal cord. It's as if the sympathetics split the PNS in development, and the PNS ended up at the top and the bottom of the cord. The rostral and caudal PNS, from this point forward, are regarded as one system, the PNS, and won't be separated again functionally or anatomically in pharmacology (this difference is explored in Neuroscience). At the ganglia is where the first synapses occur, mediated by nicotinic acetylcholine receptors.

The **SNS** exists from **T1 to L2**, originating between the vertebrae. The SNS exits the spinal cord and also forms a **sympathetic trunk**. Think of it like a spinal cord of sympathetics outside the spinal cord. The sympathetic trunk is **NOT** the ganglion. That means the sympathetic trunk is **NOT** the site of synapse. The trunk is just a clever way for sympathetic neurons originating at any level of the spine to get to any ganglion they want. SNS neurons travel out of their vertebral level into the trunk, then that same axon continues up or down the sympathetic trunk until it reaches its ganglion. At the ganglion is where the first synapse occurs, mediated by nicotinic acetylcholine receptors. Where a preganglionic neuron's axon will exit the sympathetic trunk can't be predicted; there are so many axons, it's pointless to try. But a preganglionic axon will enter the sympathetic trunk at the level of the vertebra at which it exists, and exits the trunk at the level of its ganglia.

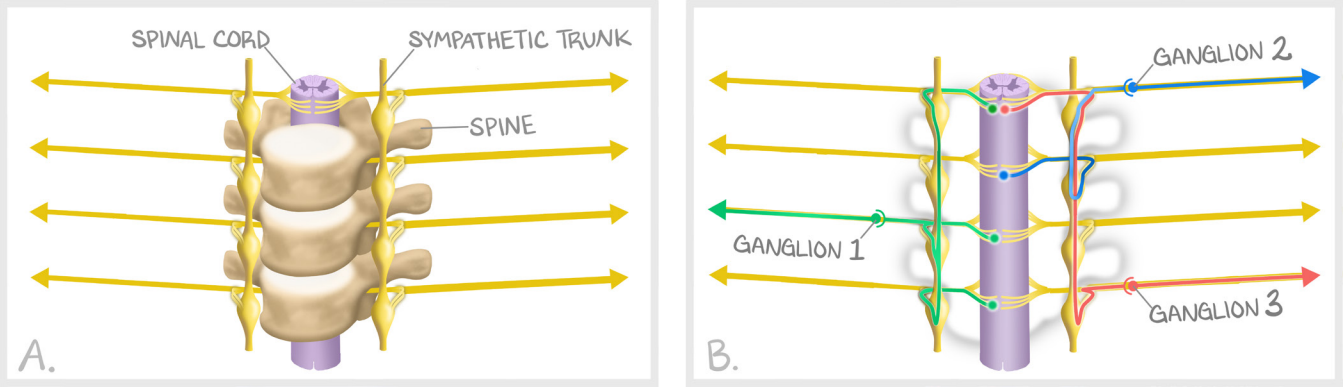

Figure 8.2: Sympathetic Trunk and Ganglia
(a) An illustration of the sympathetic trunks compared to the spinal cord. The cord is contained in the vertebrae. The sympathetic fibers originate at the level of their vertebral level, exit the spine, and enter the sympathetic trunk, a "spinal cord" of sympathetic neurons outside the cord. (b) Emphasizes that the vertebral level the fiber arises determines where that fiber will enter the sympathetic trunk, but cannot determine where it will exit.

Functionally, as we will see, the SNS has multiple means of interacting with effector organs postganglionically (function is the next section). But the SNS also has specialized **preganglionic neurons** that **do not synapse in a ganglion,** but instead synapse on the **adrenal medulla**. This synapse is the effective "preganglionic synapse," acting through nicotinic acetylcholine receptors.

The "postganglionic neuron" is no neuron, but neuroendocrine tissue that releases epinephrine. More in the next section.

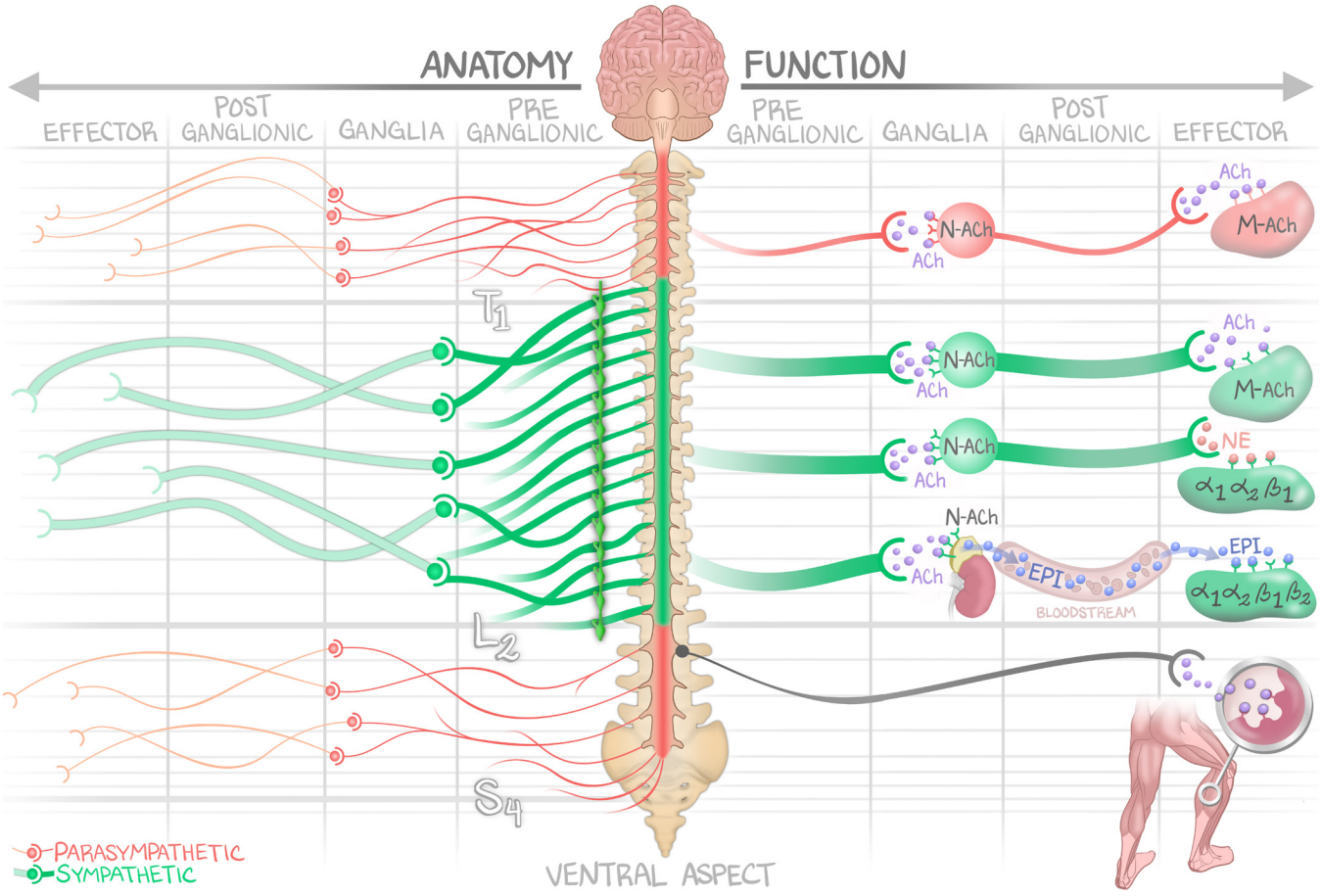

Figure 8.3: Working It Out
This is a densely packed image, and is the sum total of this lesson. On the left, the anatomy is visualized—the PNS as two independent systems, the SNS as one common one connected by a sympathetic trunk. The Thickness of the arrows represents the thickness of the nerves—the PNS are small and wispy, the SNS are thick. The similarities are shown, though, how all autonomics synapse on a ganglia before heading to their effector organ. On the right shows the variations on molecular transmission. All preganglionic neurotransmission is with ACh onto nicotinic ionotropic acetylcholine receptors. The final effector molecule is acetylcholine for the PNS, norepinephrine (norepi) or epinephrine (epi) for the SNS.

PNS Is Cholinergic by Function

Within the PNS, the **preganglionic neuron** releases **acetylcholine** at the ganglion, which binds to **nicotinic ACh receptors**. Activation of the **postganglionic neuron** sends an impulse to the effector organ. The postganglionic neuron synapses on the effector organ, communicating with **muscarinic acetylcholine receptors**. Be careful with the nomenclature. I say "nicotinic" and "muscarinic" instead of "N" and "M" because the letters sound so similar. To make the nomenclature even more confusing, nicotinic receptors are used at the **preganglionic synapse** (N_N) and also at the neuromuscular junction of **skeletal muscle** (N_M), whereas muscarinic receptors are used as **effector synapse neurotransmitters** (M_1, M_2, M_3). Using the letters N and M will get you very confused very quickly. Say the word out loud and you won't get trapped. We'll get into the specifics of the muscarinic subtypes in the next lesson. Because the PNS runs on acetylcholine (ACh), it's named the **cholinergic** system. Since skeletal muscle is under somatic control, we leave that out of the "cholinergic autonomics."

Parasympathetics influence effector organs with cholinergics—ACh.

SNS is Adrenergic by Function

In the SNS, there is a pathway where the postganglionic neuron releases ACh and the effector organ receives the signal with muscarinic ACh receptors, identical in concept to the PNS. This is illustrated in Figure 8.3 by the parasympathetic red line on top, and the first sympathetic trace in green. We won't be discussing this pathway—we want you seeing the ANS as SNS-adrenergic, PNS-cholinergic. So the OnlineMedEd version of the SNS comes next, **without** any more mention of SNS-effector muscarinic ACh receptors.

Sympathetics influence their effector organs with adrenergics—epinephrine and norepinephrine.

The only SNS synapses that we consider at the effector organ are **adrenergic,** so-called because their effect mirrors epinephrine**,** the effector molecule that comes from the adrenal medulla. Although the word adrenergic comes from the location of epinephrine release, adrenergic means activated by either the **neurotransmitter norepinephrine** (NE, or norepi) or the **circulating hormone epinephrine** (epi). The adrenergic system communicates through two different effector molecules and activates up to four receptors, the details of which are contained in #10: *Adrenergics (SNS)*.

The SNS is set up with an **immediate, short-lived neurotransmitter signal** with a **backup, long-lasting circulating hormonal signal.** At the target effector organ, SNS postganglionic neurons release **norepinephrine**. Norepi binds to and activates adrenergic receptors—α_1, α_2, and β_1. The fourth, β_2, **has no norepi innervation** and is instead activated only by circulating epinephrine.

Specialized sets of preganglionic SNS neurons do NOT synapse with a postganglionic neuron within a ganglion, but rather those first-order neurons from the CNS continue to the **adrenal medulla** where the medullary cells act as their "ganglion." These first-order neurons release acetylcholine, and the adrenal medulla has nicotinic ACh receptors, just like a ganglionic neuron. The cells of the adrenal medulla are said to be **neuroendocrine**—neuro in that they receive a signal similar to a postganglionic neuron of the ANS, and endocrine in that they release a chemical signal into the blood in response to that neural stimulus.

Be careful with memorizing this point. You should see the first-order neuron's synapsing on the adrenal medulla as the preganglionic synapse, the adrenal medulla as the "second-order-neuron," and epinephrine as the "neurotransmitter" at the effector synapse (it's really a hormone secreted into the blood, but is analogous to the postganglionic release of neurotransmitter). This becomes problematic, because you might think the adrenal medulla is the effector organ, because it's the last organ a neuron sees. But if you think of it as "the place the first-order neuron makes a synapse," it's easy to remember that the adrenal medulla is activated by **acetylcholine** and not norepi.

Epinephrine then **circulates through the body**. Although a neurotransmitter (norepi) exists only at its nerve terminal, and is transient and hyper-regulated locally, epinephrine has access to the entire circulation and lasts longer, but takes some time to make and release. Epinephrine binds α_1, α_2, β_1, and β_2. The significance of this is discussed more in #10: *Adrenergics (SNS)*. Epi has access to β_2; norepi doesn't. β_2 acts as sympathetic tone but also acts to check the norepi signal.

Physiologic Competition

The mechanisms are not going to be explained. What we want you to get out of this section is NOT receptor subtypes or intracellular mechanisms. We save that for #9: *Cholinergics (PNS)* and #10: *Adrenergics (SNS)*. But what we DO want you to learn is the key organs controlled by the autonomics, and what effect there will be if stimulated or inhibited. Each of these organ systems is dominated by a tone—all organs always have some sympathetic AND parasympathetic stimulation at the same time. But stimulating the sympathetics will do one thing, whereas stimulating the parasympathetics will do another. We want you learning what those things are, even if you cannot yet explain how they happen.

The cardiovascular system. The **parasympathetics** innervate the **nodes only** of **the heart**. Stimulation of parasympathetics activates metabotropic acetylcholine receptors and induces a **slow heart rate**. The **sympathetics** innervate the **nodal cells of the heart** the **ventricular myocytes**, and the **peripheral vasculature**. Sympathetic stimulation will **increase heart rate** (nodal cells), **increase contractility** (ventricular myocytes), and **increase systemic vascular resistance** (vascular contraction).

Activating the SNS causes ↑ HR, ↑ SVR, ↑ contractility, and bronchodilation.
Activating the PNS causes ↓ HR.

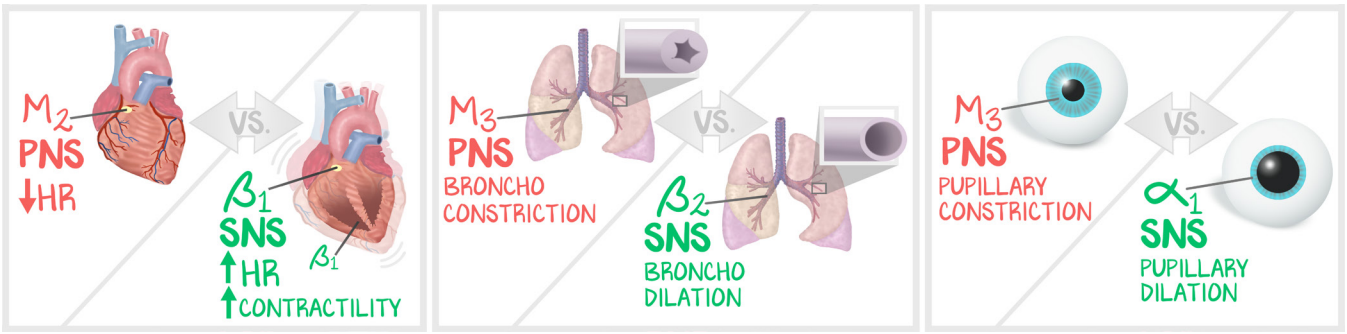

Figure 8.4: Physiologic Competition
A comparison of the opposing affects of the autonomics in the heart, the lungs, and the eye.

The Lungs. Parasympathetic innervation activates metabotropic acetylcholine receptors that cause bronchoconstriction and mucous secretion. Sympathetics activate metabotropic adrenergic receptors that induce bronchodilation.

Activating the SNS causes bronchodilation.
Activating the PNS causes bronchoconstriction and secretions.

The Eye. Parasympathetic innervation activates metabotropic acetylcholine receptors that cause **pupillary constriction** and allow for **accommodation.** Accommodation is the pupillary reflex, the change in the pupil—constriction—when the patient changes their focus from an object far away to an object very close. It is tested for by having the patient focus on the physician's finger at a distance, then moving the finger close to the patient's face—the eyes converge and the pupils should constrict. The parasympathetics innervate the **iris dilator muscle**. Pupils constrict because the iris dilator contracts. Sympathetic innervation activates metabotropic adrenergic receptors that cause **pupillary dilation** and has **no effect on accommodation**. The sympathetics innervate the **radial muscle** (when contracted, the pupil is dilated as the muscle pulls in all directions out from the center).

Activating the PNS causes pupillary constriction and permits accommodation.
Blocking the PNS causes pupillary dilation and prevents accommodation.

Activating the SNS causes pupillary dilation.
Blocking the SNS causes pupillary constriction.

	PNS		SNS	
	Agonist	**Antagonist**	Agonist	Antagonist
Pupils	Constrict	**Dilate**	Dilate	Constrict
Accommodation	Constrict	**Dilate**	Constrict	Constrict

Table 8.1: Eye Questions
This table shows the result of adding a mystery drug to an intact eye system. If you add ONE drug to a system that already has parasympathetic and sympathetic tone (a normal, intact eye), these are the responses the eye would have. Pay close attention to the fact that a PNS antagonist prevents accommodation; all other drug types keep accommodation intact.